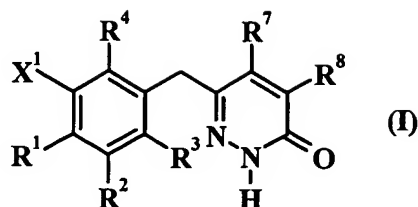


We claim:

1. A compound according to formula I



wherein;

5 X^1 is selected from the group consisting of R^5O , $R^5S(O)_n$, R^5CH_2 , R^5CH_2O , $R^5CH_2S(O)_n$, R^5OCH_2 , $R^5S(O)_nCH_2$ and NR^5R^6 ;

R^1 and R^2 are

10 (i) each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} sulfonyl, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano; or,

 (ii) taken together are $-CH=CH-CH=CH-$, or

15 (iii) taken together along with the carbons to which they are attached form a five- or six-membered heteroaromatic or heterocyclic ring with a one or two heteroatoms independently selected from the group consisting of O, S and NH;

R^3 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkylthio, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano;

20 R^4 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano;

R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, phenyl, naphthyl, pyridinyl, pyridine N-oxide, indole, indole N-oxide, quinoline, quinoline N-oxide, pyrimidinyl, pyrazinyl and pyrrolyl; wherein,

25 said alkyl and said cycloalkyl are optionally substituted with one or two substituents independently selected from the group consisting of alkyl, hydroxy, alkoxy, thiol, alkylthio, halogen, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, and dialkylamino; and,

30 said phenyl, said naphthyl, said pyridinyl, said pyridine N-oxide, said indole, said indole N-oxide, said quinoline, said quinoline N-oxide, said pyrimidinyl, said

pyrazinyl and said pyrrolyl groups are optionally substituted with one to three substituents independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ haloalkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylthio, hydroxy, halogen, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, aminoacyl, acyl, C₁₋₆ alkoxycarbonyl, carbamoyl, C₁₋₆ N-alkylcarbamoyl, C₁₋₆ N,N-dialkylcarbamoyl, nitro and cyano;

R⁶ is hydrogen, C₁₋₆ alkyl, or acyl;

R⁷ and R⁸ (i) taken independently are selected from the group consisting of hydrogen, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, amino-C₁₋₃ alkyl, C₁₋₃ alkylamino-C₁₋₃ alkyl, C₁₋₃ dialkylamino-C₁₋₃ alkyl or C₁₋₆ alkyl optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, alkoxy, thiol, alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl and halogen, N-morpholinyl; or, (ii) R⁷ and R⁸ taken together are -(CH₂)₄;

n is an integer from 0 to 2; and,

hydrates, solvates, clathrates and acid addition salts thereof.

2. A compound according to claim 1 wherein

R⁵ is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, phenyl, naphthyl, pyridinyl, pyrimidinyl, pyrazinyl and pyrrolyl; and,

said alkyl and said cycloalkyl are optionally substituted with one or two substituents independently selected from the group consisting of alkyl, hydroxy, alkoxy, thiol, alkylthio, halogen, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, and dialkylamino; and,

said phenyl, said naphthyl, said pyridinyl, said pyrimidinyl, said pyrazinyl and said pyrrolyl groups are optionally substituted with one to three substituents independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylthio, halogen, alkylamino, dialkylamino, aminoacyl, cyano, and acyl.

3. A compound according to claim 2 wherein:

X¹ is OR⁵ or SR⁵;

R³ is hydrogen or fluoro;

R⁴ is selected from the group consisting of hydrogen, chloro, fluoro and methyl;

R⁵ is optionally substituted phenyl; and,

R⁷ and R⁸ are selected from the group consisting of hydrogen, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, amino-C₁₋₃ alkyl, C₁₋₃ alkylamino-C₁₋₃ alkyl, C₁₋₃ dialkylamino-C₁₋₃ alkyl and C₁₋₆ alkyl optionally substituted with hydroxy, alkoxy, thiol, alkylthio, halogen.

5 4. A compound according to claim 3 wherein R¹ is methyl, ethyl, trifluoromethyl or halogen.

5. A compound according to claim 4 wherein R⁵ is monosubstituted phenyl.

6. A compound according to claim 4 wherein R⁵ is 2,5-disubstituted phenyl.

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7. A compound according to claim 4 wherein R⁵ is 3,5-disubstituted phenyl.

8. A compound according to claim 4 wherein R⁵ is 2,4-disubstituted phenyl.

15 9. A compound according to claim 4 wherein R⁵ is 2,6-disubstituted phenyl.

10. A compound according to claim 2 wherein:

X¹ is -OR⁵ or -SR⁵;

20 R¹ and R² are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano; and

R³ is hydrogen or fluorine.

25 11. A compound according to claim 10 wherein:

X¹ is OR⁵;

R¹ is methyl, ethyl, trifluoromethyl or halogen;

R² and R⁴ are hydrogen, fluoro, chloro, methyl or ethyl;

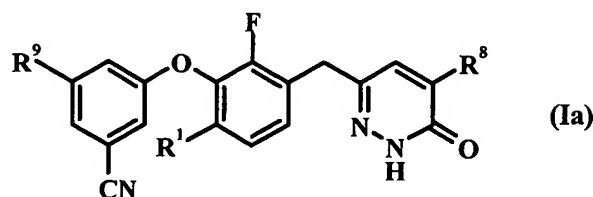
R³ is hydrogen or fluoro;

30 R⁷ is hydrogen, methyl or ethyl; and,

R⁸ is selected from the group consisting of hydrogen, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, amino-C₁₋₃ alkyl, C₁₋₃ alkylamino-C₁₋₃ alkyl, C₁₋₃ dialkylamino-C₁₋₃ alkyl and C₁₋₆ alkyl optionally substituted with hydroxy, alkoxy, thiol, alkylthio, halogen.

12. A compound according to claim 11 wherein R⁵ is monosubstituted phenyl.
13. A compound according to claim 12 wherein R⁵ is a monosubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio and C₁₋₆ haloalkoxy.
14. A compound according to claim 13 wherein R¹ is selected from the group consisting of halogen, methyl, ethyl, R³ and R⁷ are hydrogen, R⁵ is a monosubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl and C₁₋₆ haloalkyl and R⁸ is selected from the group consisting of hydrogen, methyl and ethyl.
15. A compound according to claim 11 wherein R⁵ is 2,5-disubstituted phenyl.
16. A compound according to claim 15 wherein R⁵ is a 2,5-disubstituted phenyl and the substituents are independently selected from the group consisting of halogen, cyano, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio and C₁₋₆ haloalkoxy.
17. A compound according to claim 16 wherein R¹ is selected from the group consisting of halogen, methyl, ethyl, R³ and R⁷ are hydrogen, R⁵ is a 2,5-disubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl and C₁₋₆ haloalkyl and R⁸ is selected from the group consisting of hydrogen, methyl and ethyl.
18. A compound according to claim 11 wherein R⁵ is 3,5-disubstituted phenyl.
19. A compound according to claim 18 wherein R⁵ is a 3,5-disubstituted phenyl and the substituents are independently selected from the group consisting of halogen, cyano, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio and C₁₋₆ haloalkoxy.
20. A compound according to claim 19 wherein R¹ is selected from the group consisting of halogen, methyl, ethyl, R³ and R⁷ are hydrogen, R⁵ is a 3,5-disubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl and C₁₋₆ haloalkyl and R⁸ is selected from the group consisting of hydrogen, methyl and ethyl.

21. A compound according to claim 20 with formula Ia wherein:



R¹ is selected from the group consisting of fluoro, chloro, bromo and methyl;

R⁸ is selected from the group consisting of hydrogen, methyl and ethyl;

5 R⁹ is selected from the group consisting of C₁₋₆ alkyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, halogen and cyano.

22. A compound according to claim 11 wherein R⁵ is 2,4-disubstituted phenyl.

10 23. A compound according to claim 22 wherein R⁵ is a 2,4-disubstituted phenyl and the substituents are independently selected from the group consisting of halogen, cyano, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio and C₁₋₆ haloalkoxy.

15 24. A compound according to claim 23 wherein R¹ is selected from the group consisting of halogen, methyl, ethyl, R³ and R⁷ are hydrogen, R⁵ is a 2,4-disubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl and C₁₋₆ haloalkyl and R⁸ is selected from the group consisting of hydrogen, methyl and ethyl.

25. A compound according to claim 11 wherein R⁵ is 2,6-disubstituted phenyl.

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26. A compound according to claim 25 wherein R⁵ is a 2,6-disubstituted phenyl and the substituents are independently selected from the group consisting of halogen, cyano, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₃₋₈ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio and C₁₋₆ haloalkoxy.

25 27. A compound according to claim 26 wherein R¹ is selected from the group consisting of halogen, methyl, ethyl, R³ and R⁷ are hydrogen, R⁵ is a 2,6-disubstituted phenyl and the substituent is selected from the group consisting of halogen, cyano, C₁₋₆ alkyl and C₁₋₆ haloalkyl and R⁸ is selected from the group consisting of hydrogen, methyl and ethyl.

30 28. A compound according to claim 11 wherein R⁵ is a 2,3,5-trisubstituted phenyl.

29. A compound according to claim 1 wherein:

X^1 is OR^5 or SR^5 ;

R^3 and R^4 are selected from the group consisting of hydrogen, chloro, fluoro, and methyl;

R^5 is optionally substituted pyridinyl, pyridine N-oxide, indole, indole N-oxide, quinoline,
quinoline N-oxide, pyrimidinyl, pyrazinyl and pyrrolyl.

30. A compound according to claim 1 wherein R^1 and R^2 along with the carbon atoms to which they are attached form a phenyl, dihydropyran, dihydrofuran or furan ring.

31. A compound according to claim 30 wherein:

X^1 is OR^5 or SR^5 ;

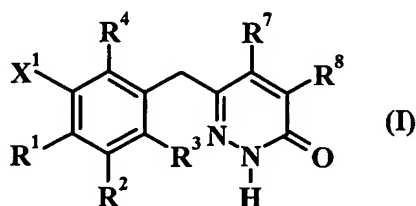
R^3 , and R^7 are hydrogen;

R^4 is hydrogen or fluoro;

R^8 is hydrogen or methyl; and,

R^5 is optionally substituted phenyl.

32. A method for treating an HIV infection, or preventing an HIV infection, or treating AIDS or ARC, comprising administering to a host in need thereof a therapeutically effective amount of a compound of formula I



wherein,

X^1 is selected from the group consisting of R^5O , R^5S , R^5CH_2 , R^5CH_2O , $R^5CH_2S(O)_n$, R^5OCH_2 , $R^5S(O)_nCH_2$, NR^5R^6 and $R^5C(=O)$;

R^1 and R^2 are

- (i) each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} sulfonyl, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano; or,
- (ii) taken together are $-CH=CH-CH=CH-$, or

(iii) taken together along with the carbons to which they are attached form a five- or six-membered heteroaromatic or heterocyclic ring with a one or two heteroatoms independently selected from the group consisting of O, S and NH;

R³ and R⁴ are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano;

R⁵ is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, phenyl, naphthyl, pyridinyl, pyrimidinyl, pyrazinyl and pyrrolyl; wherein,

said alkyl and said cycloalkyl are optionally substituted with one or two substituents

independently selected from the group consisting of alkyl, hydroxy, alkoxy, thiol, alkylthio, halogen, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, and dialkylamino; and,

said phenyl, said naphthyl, said pyridinyl, said pyrimidinyl, said pyrazinyl and said pyrrolyl groups are optionally substituted with one to three substituents

independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylthio, hydroxy, halogen, amino, alkylamino, dialkylamino, aminoacyl, acyl, alkoxycarbonyl, carbamoyl, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, nitro and cyano;

R⁶ is hydrogen, C₁₋₆ alkyl, or acyl;

R⁷ and R⁸ (i) taken independently are selected from the group consisting of hydrogen, , amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, amino-C₁₋₃ alkyl, C₁₋₃ alkylamino-C₁₋₃ alkyl, C₁₋₃ dialkylamino-C₁₋₃ alkyl or C₁₋₆ alkyl optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, alkoxy, thiol, alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ sulfonyl and halogen, N-morpholinyl; or, (ii) R⁷ and R⁸ taken together are -CH=CH-CH=CH- or -(CH₂)₄;

n is an integer from 0 to 2; and,

hydrates, solvates, clathrates and acid addition salts thereof.

33. A method according to claim 32 wherein:

X¹ is OR⁵;

R¹ is methyl, ethyl, trifluoromethyl or halogen;

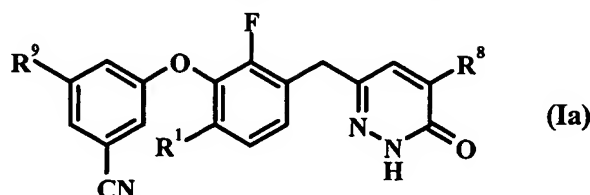
R² and R⁴ are independently hydrogen, fluoro, chloro, methyl or ethyl;

R³ is hydrogen or fluoro; and,

R⁵ is optionally substituted phenyl;

R⁷ is hydrogen, methyl or ethyl.

34. A method according to claim 33 comprising administering a compound of formula **Ia** wherein



5 R¹ is selected from the group consisting of fluoro, chloro, bromo and methyl;

R⁸ is selected from the group consisting of hydrogen, methyl and ethyl;

R⁹ is selected from the group consisting of alkyl, cycloalkyl, haloalkyl, halogen and cyano.

35. A method for treating HIV infection according to claim 32 further comprising co-administering at
10 least one compound selected from the group consisting of HIV protease inhibitors, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, CCR5 inhibitors and viral fusion inhibitors.

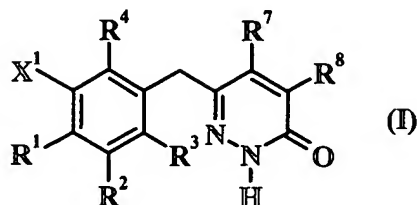
36. A method according to claim 35 wherein the reverse transcriptase inhibitor is selected from the
15 group consisting of zidovudine, lamivudine, didanosine, zalcitabine, stavudine, rescriptor, sustiva and viramune, efavirenz, nevirapine or delavirdine and/or the protease inhibitor is selected from the group consisting of saquinavir, ritonavir, nelfinavir, indinavir, amprenavir, lopinavir.

37. A method for inhibiting a retrovirus reverse transcriptase comprising administering a compound
20 according to claim 32.

38. A method according to claim 37 wherein the host is infected with a strain of HIV expressing a reverse transcriptase with at least one mutation compared to wild type virus.

25 39. A method according to claim 32 wherein said strain of HIV exhibits reduced susceptibility to efavirenz, nevirapine or delavirdine.

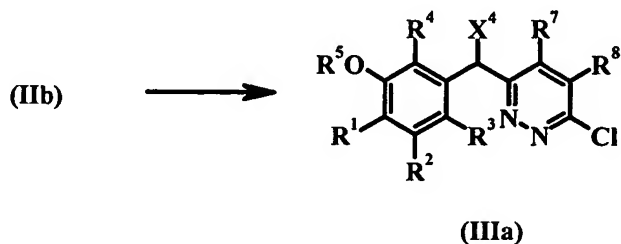
40. A pharmaceutical composition comprising a therapeutically effective quantity of a compound of formula I



wherein:

- 5 X^1 is selected from the group consisting of R^5O , $R^5S(O)_n$, R^5CH_2 , R^5CH_2O , $R^5CH_2S(O)_n$, R^5OCH_2 , $R^5S(O)_nCH_2$ and NR^5R^6 ;
 R^1 and R^2 are
- (i) each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} sulfonyl, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano; or,
 - 10 (ii) taken together are $-CH=CH-CH=CH-$, or
 - (iii) taken together along with the carbons to which they are attached form a five- or six-membered heteroaromatic or heterocyclic ring with a one or two heteroatoms independently selected from the group consisting of O, S and NH;
- 15 R^3 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkylthio, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano;
- R^4 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, halogen, amino, alkylamino, dialkylamino, aminoacyl, nitro and cyano;
- 20 R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, phenyl, naphthyl, pyridinyl, pyrimidinyl, pyrazinyl and pyrrolyl; wherein,
- said alkyl and said cycloalkyl are optionally substituted with one or two substituents independently selected from the group consisting of alkyl, hydroxy, alkoxy, thiol, alkylthio, halogen, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, and dialkylamino;
 - 25 and,
 - said phenyl, said naphthyl, said pyridinyl, said pyrimidinyl, said pyrazinyl and said pyrrolyl groups are optionally substituted with one to three substituents independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} sulfonyl, C_{1-6} haloalkoxy, C_{1-6} haloalkylthio, hydroxy,
 - 30

(iii) treating a compound of formula **IIb** with base and condensing the conjugate base of **IIb** (X^4 = alkoxycarbonyl or CN) with a pyrazine compound to produce a compound of formula **IIIa**;



(iv) cleaving the alkoxycarbonyl or nitrile by acidic or basic hydrolysis, decarboxylating the resulting carboxylic acid and hydrolysing the chloropyrazine to a pyridazinone of formula **I**.

42. A process according to claim 41 wherein said ether is formed by coupling an arylboronic acid and **IIa** in the presence of a copper (II) salt.
43. A process according to claim 41 wherein said ether is formed by coupling an aryl halide and **IIa** in the presence of a copper (I) salt.
44. A process according to claim 41 wherein said ether is formed by coupling an alkyl halide, an aralkyl halide or aryl halide and said aryl halide being substituted with electronegative groups and **IIa**, said coupling being base-catalyzed.
45. A process according to claim 41 wherein said ether is formed by coupling an alcohol and **IIa** said coupling is catalyzed an a dialkylazodicarboxylate and triaryl or trialkylphosphine.
46. A process according to claim 41 wherein said base is sodium hydride and said pyrazine compound is a 3,6-dihalopyrazine or a 3-halo-6-alkoxypyrazine.
47. A process according to claim 41 wherein said base is a sodium alkoxide and said pyrazine derivative is a 3,6-dihalopyrazine or a 3-halo-6-alkoxypyrazine.
48. A process according to claim 41 wherein said acidic hydrolysis conditions comprise a carboxylic acid and an aqueous hydrohalic acid.

49. A process according to claim 48 where said carboxylic acid is acetic acid and said hydrohalic acid is hydrochloric acid.

50. A process according to claim 49 said process further comprising sodium acetate.

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51. A process according to claim 41 wherein said alkoxycarbonyl is saponified with base and said chloropyrazine is hydrolyzed by a carboxylic acid and an aqueous hydrohalic acid

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